Laboratory Medicine Update

March 2019

On-Site Urinary 5-HIAA and HVA/VMA Mass Spectrometry Testing

We are notifying you that on Monday the 18th of March 2019, the Clinical Mass Spectrometry Laboratory at the Health Science Center will begin on-site testing of urinary 5-HIAA and HVA/VMA.

Four orderable tests will be available:

Test Name	Aliases	Provincial Mnemonic
5-Hydroxyindoleacetic acid, random urine	5-HIAA; serotonin metabolite	HI5UP
5-Hydroxyindoleacetic acid, 24h urine		HI5U24HP
Homovanillic acid/Vanilylmandelic acid, random urine	HVA/VMA; catecholamine metabolites	VMAHVAUP
Homovanillic acid/Vanilylmandelic acid, 24h urine		VMAHVACU24P

The testing will normally be performed every 2 weeks. Approval for STAT request requires approval by the clinical biochemist on-call. All of these parameters are affected by various dietary components and drugs; hence some restrictions are advised. A listing of patient diet and medication restrictions required for the accuracy of test results as well as other patient collection instructions can be found at: http://www.easternhealth.ca/OurServices.aspx?d=2&id=367&p=162

The 24h urine collection is always the preferred specimen for analysis. Random urine collection should only be an alternative in special circumstances when the 24h urine collection cannot be obtained. Nevertheless, minimal diurnal variation in HVA/VMA urinary excretion and the positive correlation of HVA/VMA random urine with 24h urine testing allows the convenient use of random urine specimens.

Diagnostic investigation and monitoring by analysis of urinary 5-HIAA and HVA/VMA by stable isotope dilution ESI-UPLC-MS/MS method of respectively carcinoid tumors and neuroblastoma.

Carcinoid tumors:

Carcinoid tumors belong to a subset of tumors called neuroendocrine tumors (NETs), which usually begin in the digestive tract, the lungs or the thymus. Diagnosis of carcinoid tumors involve the assessment of clinical symptoms, hormone levels, histology and imaging.

Serotonin secreted by some neuroendocrine tumor cells is converted by the liver and the lungs to **5-HIAA** which is then excreted in the urine. Urinary measurement of 5-HIAA has a clinical sensitivity and specificity of 50-80% and 97%, respectively, for carcinoid tumor diagnosis. Urinary 5-HIAA measurement has better sensitivity for primary midgut carcinoid tumors. But urinary 5-HIAA excretion, up to 150 µmol/day, may be found in patients with malabsorption syndromes, such as celiac and Whipple's disease and in otherwise healthy individuals after the ingestion of tryptophan- or serotonin-rich foods. A 24h urinary 5-HIAA analysis should be performed for all patients with a small intestine primary neuroendocrine tumor, as well as those with symptoms suggestive of the carcinoid syndrome (i.e. flushing, diarrhea, facial spider nevi, cardiac arrhythmia and predominantly right-sided cardiac failure). Urinary 5-HIAA concentration rise in parallel with serotonin production, without any obvious signs of saturation of the metabolic pathway making it also suitable as a monitoring test. Urinary serotonin measurements are of value in patients with foregut and hindgut carcinoid tumors showing no elevation of urinary 5-HIAA.

Neuroblastoma:

Neuroblastoma arises from early neural crest precursor cells that undergo transformation secondary to genetic or epigenetic events and lead to blocked or aberrant developmental differentiation. Familial cases represent less than 2% of all cases. Unlike pheochromocytoma, neuroblastoma is almost exclusive to children, accounting for approximatively 7-10% of childhood cancers, and representing the most diagnosed malignancy in the first year of life. Patients with localized disease can be asymptomatic, whereas children with advanced disease appear ill at presentation, usually with systemic symptoms. Diagnosis of Neuroblastoma can be made by:

1. Histologic confirmation on histopathology, supplemented by immunohistochemistry, with or without elevations of catecholamine metabolites (HVA/VMA),
2. Bone marrow aspirate or trephine biopsy containing unequivocal tumor cells with elevations of HVA/VMA.

Combined **HVA/VMA** urinary measurements has a clinical sensitivity and specificity of 80% and 95%, respectively, for neuroblastoma diagnosis. Urinary HVA/VMA testing can be used for monitoring disease response or recurrence. VMA is **not** the analyte of choice for investigation of paraganglioma and pheochromocytoma. We recommend starting with urine metanephrines for better clinical sensitivity.

New reference interval for urinary 5-HIAA, HVA and VMA.

5-HIAA (per day)

Sex	Age interval	Reference interval
M/F	≥ 15 years	<40.0 µmol/Day

5-HIAA (per creatinine)

Sex	Age interval	Reference interval
M/F	0-<5 years	<13.0 µmol/mmol creatinine
M/F	≥ 5 years	<10.0 µmol/mmol creatinine

VMA (per day)

Sex	Age interval	Reference interval
M/F	≥ 15 years	<36.0 µmol/Day

VMA (per creatinine)

Sex	Age interval	Reference interval
M/F	0-<2 years	<11.0 µmol/mmol creatinine
M/F	2-<5 years	<6.5 µmol/mmol creatinine
M/F	5-<15 years	<5.0 µmol/mmol creatinine
M/F	≥ 15 years	<4.0 µmol/mmol creatinine

HVA (per day)

Sex	Age interval	Reference interval
M/F	≥ 15 years	<49.0 µmol/Day

HVA (per creatinine)

Sex	Age interval	Reference interval
M/F	0-<1 year	<21.7 µmol/mmol creatinine
M/F	1-<2 years	<14.3 µmol/mmol creatinine
M/F	2-<5 years	<9.5 µmol/mmol creatinine
M/F	5-<10 years	<8.4 µmol/mmol creatinine
M/F	10-<15 years	<6.0 µmol/mmol creatinine
M/F	≥ 15 years	<5.6 µmol/mmol creatinine

References

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